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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of :

Edwin Mellor SOUTHERN et al. :

Serial No. NEW : **Attn: Application Branch**

Filed April 26, 2000 : **Attorney Docket No. 2000-0541**

METHODS OF DETERMINING POLYNUCLEOTIDE INTRAMOLECULAR STRUCTURE (AS AMENDED)
(Rule 1.53(b) Divisional of Serial No. 08/676,140, Filed October 2, 1996)

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

Kindly amend the application as follows:

IN THE SPECIFICATION

Page 1, line 5, delete in its entirety and replace with --BACKGROUND OF THE INVENTION --;

line 6, insert -- 1. Field of the Invention --;

line 10, change ": for" to -- . For --;

line 22, change "interaction" to -- interactions --;

between lines 23-24, insert the following heading -- 2. Description of Related Art --.

Page 2, line 8, change ":" to -- ; --;

line 15, change "two" (first occurrence) to -- to --;

line 19, delete in its entirety and replace with -- SUMMARY OF THE INVENTION --.

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Page 3, before line 1, insert the following:

-- BRIEF DESCRIPTION OF THE FIGURES

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Fig. 1 is an illustration of an array of all tetranucleotides.

Figs. 2(a) and (b) depict scanning arrays of oligonucleotide precursors applied in a circular patch.

Fig. 3 shows hybridisation of $tRNA^{phe}$ to an array of type $N_3X_2N_3$.

Fig. 4 shows the effect of including non-radioactive oligonucleotides with the tRNA target in a hybridisation solution.

Fig. 5 shows the sites of hybridisation of cooperative antisense oligonucleotides to the structure of rabbit β-globin mRNA.

Fig. 6 shows four arrays of complements to a region of human CFTR gene.

Fig. 7(a) shows a folded structure of the Rev response element (RRE) of HIV RNA derived from computer molecular modelling. Figs. 7(b) and (c) show the hybridisation of labelled RRE HIV RNA to two universal arrays.

Figs. 8 (a), (b) and (c) show scanning arrays of the region of RRE analyzed in Fig. 7.

Figs. 9(a) and (b) show the analysis described in Fig. 8 conducted to presence of neomycin.

Figs. 10(a) and (b) show the effect of magnesium ions on the folding behavior of RNAs.

Figs. 11(a), (b) and (c) show the analysis of the TAR element of HIV using the method of this invention.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT(S) --.

Page 4, line 3, change "targetted" to -- targeted --.

Page 20, line 23, delete in its entirety and replace with -- Figures 7(a)-7(c). --.

Page 22, line 1, delete in its entirety and replace with -- Figures 8(a)-8(c). --;

line 11, delete "[";

line 14, delete "]";

line 16, delete in its entirety and replace with -- Figures 9(a)-9(b). --;

line 25, delete in its entirety and replace with -- Figures 10(a)-10(b). --;

line 35, delete in its entirety and replace with -- Figures 11(a)-11(c). --.

IN THE CLAIMS

Cancel without prejudice claims 1-13 and substitute therefor the following new claims:

-- 14. A method of studying a tertiary structure of a target which is a polymeric molecule having a known sequence, which method comprises providing a plurality of different ligands in the form of an array on a solid surface, said different ligands being complementary to different segments of the target; applying the target in solution to the array of ligands under conditions which preserve the tertiary structure of the target; and observing quantitative differences between interactions of the target with the different ligands of the array; provided that, when the ligands are not oligonucleotides or oligonucleotide analogues, then the target is a nucleic acid.

15. A method of determining combinations of ligands specific for a target, which method comprises the steps of:

a) binding at least one ligand to the target, to form a target complex,

b) applying the target complex to other ligands which form an array on a solid surface, under conditions which allow interaction between the other ligands and the target complex, and

c) identifying at least one other ligand which interacts with the target complex.

16. The method as claimed in claim 15, comprising the additional step of binding the at least one other ligand to the target complex and then repeating steps b) and c).

17. The method as claimed in claim 15, wherein one ligand is an oligonucleotide or oligonucleotide analogue and another ligand is a peptide.

18. The method as claimed in claim 15, wherein two ligands are joined together by means of a linker.

19. The method as claimed in claim 15, wherein the at least one ligand to be bound to the target to form a target complex in step a), is chosen by mixing the target with a library of ligands and choosing from the library at least one ligand that binds to the target.

20. The method as claimed in claim 14, wherein the ligands are oligonucleotides or oligonucleotide analogues.

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21. The method as claimed in claim 15, wherein the ligands are oligonucleotides or oligonucleotide analogues.

22. The method as claimed in claim 20, wherein the ligands are oligonucleotide analogues modified by the addition or substitution of other chemical moieties selected from oligoaliphatic ethers, intercalating agents, positively charged residues, chelating agents and lipophilic agents.

23. The method as claimed in claim 21, wherein the ligands are oligonucleotide analogues modified by the addition or substitution of other chemical moieties selected from oligoaliphatic ethers, intercalating agents, positively charged residues, chelating agents and lipophilic agents.

24. The method as claimed in claim 20, wherein the ligands form the basis of a ribozyme.

25. The method as claimed in claim 21, wherein the ligands form the basis of a ribozyme.

26. The method as claimed in claim 14, wherein the target and one or more ligands are different chemical types.

27. The method as claimed in claim 15, wherein the target and one or more ligands are different chemical types.

28. The method as claimed in claim 14, wherein at least one ligand becomes covalently bound to the target.

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29. The method as claimed in claim 15, wherein at least one ligand becomes covalently bound to the target.

30. The method as claimed in claim 15, wherein the target is a molecule having a secondary or tertiary structure, and is caused to interact with the array of ligands under conditions such that the secondary or tertiary structure is retained. --

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IN THE SEQUENCE LISTING

Please transfer the paper and computer readable copies of the Sequence Listing from the parent application Serial No. 08/676,140 filed October 2, 1996 to the present application. The Sequence Listing of the present application is identical to the parent application, and the paper and computer readable copies of the Sequence Listing in the parent application are identical to each other. No new matter was added to the Sequence Listing in the parent application, and thus, no new matter is added to the Sequence Listing of the present application.

IN THE ABSTRACT

Kindly insert the attached separate sheet of abstract at the end of the application in its appropriate location.

REMARKS

The foregoing amendments cancel original claims 1-13 and add new claims 14-30. New claims 14-30 represent the subject matter to be prosecuted in this divisional application. In addition, the specification has been amended along the lines of the parent application.

Favorable action on the merits is solicited.

Respectfully submitted,

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